REMARKS

**I. Status of Claims**

Claims 4-16 of the claims are withdrawn.

Claims 1-3, 17-19 and 21-22 are pending.

**II. Meola et al. Does not Anticipate Claims 1-3, 17 and 21 Because Meola does Not Teach all the Claimed Elements.**

Claims 1-3, 17, 21 were rejected under 35 U.S.C. § 102(b) over Meola et al.

Because claim 1 is an independent claim and claims 2-3, 17, 21 depend on claim 1, what holds below for claim 1, holds for all rejected claims.

Meola does not anticipate claims 1-3, 17 and 21 because this publication does not teach all the elements in the pending claims, as required by case law. An anticipating prior art reference should disclose ***each and every limitation of the claim*** expressly or inherently. *Akamai Techs. v. Cable & Wireless Internet Servs.*, 344 F.3d 1186, 1192 (Fed. Cir., 2003). To anticipate a claim, ***a reference must disclose every element of the challenged claim*** and enable one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996) *(emphasis added)*.

The examiner tries to force elements of Meola to match elements of the pending claims, but the matches are incorrect (see page 2, par. 2 of the Office Action). The examiner continues to try to force equating "mimotopes" with the peptides of the present invention, but there is no fit.

Meola's stated goal is "To test if these mimotopes could be useful in developing a vaccine against human hepatitis B virus (HBV)." (p. 3162) Meola's conclusion refers to mimotopes "identified from random peptide libraries...could be important leads for the derivation of new vaccines." Meola reported peptides with viral immunogenic carriers used for immunization.

A "mimotope" means the structure "mimics" some structure of relevance (the relevance determined by the study parameters). A mimotope could be of a chemical nature similar to a native biological structure, or quite different chemically. As an example of the latter, a peptide sequence could be determined from the phage display of peptide sequences that bind to an antibody that was originally produced to a carbohydrate structure (or lipid, or any chemical structurally different from the peptide mimotope). The reason for the latter binding is that, in the universe of chemical structures, many will have the size to "fit" within an antibody combining site and will have atomic compositions capable of forming sufficient non-covalent binding interactions within the antibody combining site to yield a discernible, measurable, assayable affinity.

Thus, discerning a mimotope for any protein binding to selected members of the phage peptide display library as did Meola does not provide the chemical nature of the "natural" binding partner of the protein. For antibody binding, the natural immunogen structure eliciting the particular antibody, could be quite different than the mimotope peptide structure.

In the Meola report, the mimotopes were selected for study on the basis of having homologous, not identical, sequences to the hepatitis virus surface antigen. Those mimotopes were then conjugated in different ways to several proteins and a MAP platform, used to immunize mice and rabbits, and the immune sera obtained was characterized as to reactivities (antibody binding) to the hepatitis surface antigen. The authors concluded that mimotope identification, followed by preparation of immunogens containing the mimotope sequences, could yield antigens to be used as vaccines possibly effective in protecting individuals against various pathogens. These mimotopes do not have all the elements of claim 1.

**1. There is no "target protein" expressed in Meola.**

Even assuming that HbsAg is the "target protein" required by claim 1, as the examiner believes, none of the sequences of Meola are identical to "a contiguous amino acid peptide region" of the sequence of the target as they must be to satisfy claim 1(b). (see Meola, Fig. 1) Meola has mimotopes that are not identical to a contiguous sequence of the target protein as required in claim 1(b), "do not show any sequence similarity with the natural Ag" and "show similarity" with 121-127 of HBsAg. "They probably mimic a nonlinear epitope of HbsAg." (page 3169) In fact, Meola teaches away from using a pathogen's primary structure, in contrast to the present invention which starts with the amino acid sequence of the target protein, and derives peptides therefrom.

Referring to disease specific mimotopes, Meola states:

> This information is not readily available by studying the pathogen structure because the immune system reacts to the Ags in a complex way that has to do with presentation and processing.

Meola, page 3162.

A mimotope does not use the linear sequence of pathogen for immunization.

> It became clear that the conformation of the peptide as displayed on the phage is important for immunization.

Meola, page 3163.

Not surprisingly, the exact primary sequence of any 5-10 amino acid contiguous sequences of the hepatitis antigen is not used in the immunization procedures or experiments of Meola, as required in present claim 1(a).

**2. There is no "comparative protein" as required by claim 1(d, e) in Meola;**

The examiner decided that:

> Mimotopes 13 and 35 are the selected immunogenic peptides as the **comparative proteins** from phage library. (*emphasis provided, sic)*
>
> (See Office Action page 2, par. 2)

Mimotopes 13 and 35 do not fit the definition of comparative proteins which are selected for present claim 1(d, e), because Meola's mimotopes are all derived from the same HbsAg antigen, whereas comparative proteins of the present invention are from different antigens than a "target protein", and are selected to minimize cross reactivity of antibodies designed to react with the target protein.

What is argued in the Action is the examiner's opinion. Meola never expressly states "comparative protein" nor are mimotopes proteins. Comparative proteins in the pending claims have a different definition: as stated above and in the specification, comparative proteins are selected from some defined set of proteins examined for potential homologies; those with homolgies as defined in claim 1 are then **excluded** in the **claimed** procedures.

**3. Mimotopes of Meola are proteins which are larger than 5-10 amino acids because they include viral carriers.**

Even if HbsAg sequence 120-132 is a "selected peptide", as the examiner believes, 12 amino acids is outside the scope of claim 1(a).

**4. Meola teaches away from peptides of the present claims.**

> Thus, the definition of a mimotope, particularly an immunogenic mimotope (i.e., a molecule capable of eliciting Abs to the original Ag it is supposed to mimic), in most cases cannot be reduced to the description of a short peptide, leaving aside the molecular context in which it is first identified.

Meola, page 3170.

**III. A Prima Facie Case of Obviousness is not Established Because Rejections Based on Meola are Faulty, Therefore, Meola Must be Removed as a Basis**

**for the 103 Rejections.**

Claims 18-19 were rejected under 35 U.S.C. §103(a) over Meola et al in view of Hasegawa et al.

Claim 22 was rejected under 35 USC §103 over Meola and Tu.

Because, as shown in Section II herein, Meola does not teach the peptides of the present invention, these 103 rejections must fall also.

Hasegawa merely teaches adjuvants. There is no teaching or suggestion to combine Meola and Hasegawa. Even if Meola and Hasegawa were combined, the combination does not render claims 18-19 obvious because neither Meola nor Hasegawa teach or suggest a plurality of immunogenic peptides that fits the description of claim 1.

On page 4 of the Action, the examiner states that Meola in view of Tu (US Pat 5674483) renders claim 22 obvious. Tu merely teaches a method of administering IL-12 to reduce inflammation. IL-12 is a "heterodimeric cytokine" exceeding the limits of claim 1 (Howard *et al.* Chap. 20, Fundamental Immunology)

In *Nursery Supplies*, the court held:

> One **cannot simply backtrack from the invention to find a connection** to the prior art. Hindsight must be avoided. See *W.L. Gore and Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983). Rather, **one must start with the prior art and find some suggestion or motivation either in a single reference** to modify it to produce the claimed invention, or some suggestion or motivation in a group of references to combine them to produce the claimed invention. *Nursery Supplies v. Lerio Corp.*, 45 U.S.P.Q.2d (BNA) 1332 (M.D. Pa. Sept. 19, 1997). (*emphasis added*).

There is no teaching or suggestion to combine Meola and Tu. Even if Meola and Tu were properly combined, the combination does not produce claim 22 because Meola does not teach or suggest an immunogenic peptides that fit the description of claim 1, and Tu only teaches IL-12.

It is to be noted, however, that citing references which **merely indicate that isolated elements and/or features** recited in the claims are known **is not a sufficient basis** for concluding that the combination of claimed elements would have been obvious. *Ex parte Hiyamizu* (BPAI 1988) 10 PQ. 2d 1393 (*emphasis added*).

Even if all of the elements of a claim are present in the prior art, the claim will not be obvious unless the prior art also contained, at the time the claim was filed, a motivation to combine prior art elements into the claimed invention. The conclusion that the prior art contained a motivation to combine is a conclusion of fact. *Scimed Life Sys. v. Johnson & Johnson*, 2004 U.S. App. LEXIS 510.

Obviousness requires **a suggestion of all limitations** in a claim." *CFMT, Inc. v.*

*YieldupInt'l Corp.*, 2003 U.S. App. LEXIS 23072 (Fed. Cir. 2003) (*emphasis added*).

To properly combine two references to reach a conclusion of obviousness, there must be some teaching, suggestion or inference in either or both of the references, or knowledge generally available to one skilled in the art, which would have led one to combine the relevant teachings of the two references. *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc. et al.* (CAFC 1985) 776 F. 2d 281, 227 USPQ 657; *Ex parte Levengood, supra.* Both the suggestion to make the claimed composition or device or carry out the claimed process and the reasonable expectation of success must be founded in the prior art, not in applicant's disclosure. *In re Vaeck* (CAFC 1991) 947 F. 2d 488, 20 PQ. 2d 1438. The references, viewed by themselves and not in retrospect, must suggest doing what applicant has done. *In re Shaffer* (CCPA 1956) 229 F. 2d 476, 108 USPQ 326; *In re Skoll* (CCPA 1975) 523 F. 2d 1392, 187 USPQ 481.

In *re Rouffet,* the court held

To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court **requires the examiner to show a motivation to combine the references that create the case of obviousness**. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed. In *re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998). (*emphasis added*).

Therefore, Claims 18-19, and 22 are not obvious over Meola in view of either Hasegawa or Tu.

## V. Conclusion and Summary

In view of the arguments presented herein, please allow all pending claims. If there are still issues, an interview is requested.

No fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21417/92378).

Respectfully submitted,

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